Incidental adrenal masses are being discovered with greater frequency because of the increased use and improved quality of cross-sectional imaging [1]. These lesions, known as “adrenal incidentalomas” (AIs), refer to unsuspected adrenal masses 1 cm or larger that are detected on imaging studies, excluding studies of patients who are being evaluated for cancer [2].

AIs present diagnostic challenges for both radiologists and referring clinicians, particularly when the initial imaging characteristics are nonspecific. Although most AIs are benign, some may prove to be hormone secreting, malignant, or both. The American College of Radiology (ACR) [2, 3], the American Association of Clinical Endocrinologists, the American Association of Endocrine Surgeons [4], and the National Institutes of Health (NIH) [5] have independently developed guidance in the workup of AIs.

In this article, we provide a brief review of adrenal mass imaging and a discussion of the primary imaging and clinical guidelines, including their key similarities and differences. We suggest an alternative approach to the imaging and clinical workup of AIs that combines the imaging expertise of the ACR and the clinical expertise of the American Association of Clinical Endocrinologists, the American Association of Endocrine Surgeons, and the NIH. Finally, we provide sample radiology report dictations that have been developed at our institution to provide consistency in follow-up recommendations for AIs.

Imaging Features of Common Incidental Adrenal Nodules

An understanding of the typical imaging features of adrenal masses is critical in determining proper categorization of and management recommendations for such masses. We present a brief summary of these features. Excellent reviews that provide a more detailed overview of adrenal mass imaging are also available elsewhere [6–9].

Most AIs, including adrenal adenoma, myelolipoma, hemorrhage, and cyst, display specific imaging findings that allow for confident diagnosis with the use of CT and MRI. Adrenal adenoma is the most common AI, and 70% of cases contain significant amounts of intracellular lipid [1, 10]. The presence of intracellular lipid (i.e., lipid-rich adenoma) allows differentiation from lipid-poor adenomas and nonadenomas with high specificity [11–13]. Adrenal mass characterization with the use of CT requires placing an ROI over one-half to two-thirds of the surface area of the mass while avoiding areas of necrosis and calcification [6, 8, 9, 11, 12] (Figs. 1A and 1D–1F). An attenuation value of less than 10 HU on unenhanced CT is highly specific for the diagnosis of lipid-rich adenomas (Fig. 1A) [12]. Similarly, chemical selective MRI performed using in-phase and opposed-phase gradient-echo sequences is highly specific for the diagnosis of lipid-rich adenomas because it reveals reduced signal intensity on opposed-phase sequences relative to in-phase sequences [14] (Figs. 1B and 1C).

Adrenal protocol CT performed without contrast administration, followed by acquisition

Keywords: adrenal, adrenal adenoma, adrenal incidentaloma, incidental adrenal mass, incidental adrenal nodule

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OBJECTIVE. A variety of imaging and clinical guidelines have been developed to assist radiologists and referring physicians in the workup of incidental adrenal masses. The objective of this article is to provide a concise review of incidental adrenal mass imaging and present the key differences between the available guidelines.

CONCLUSION. An alternative algorithm for the imaging and clinical workup of adrenal incidentalomas is presented in an attempt to bridge sometimes conflicting recommendations.
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of images at 70–80 seconds and at 15 minutes after contrast administration, uses characteristics of contrast washout to differentiate adenomas from nonadenomas [1, 15, 16] (Figs. 1D–1F). This is particularly helpful for identifying lipid-poor adrenal adenomas, which can appear similar to nonadenomas on unenhanced CT and chemical selective MRI. Adenomas display rapid contrast washout at 15 minutes, whereas nonadenomas typically undergo slow contrast washout [15–18].

Myelolipomas contain macroscopic fat, which is characterized by attenuation of less than −20 HU on CT and signal dropout on fat-suppressed MRI sequences [19–21] (Fig. 2). Macroscopic fat rarely can be seen in adrenal adenomas, adrenocortical carcinomas (ACCs), and pheochromocytomas, and large myelolipomas may be difficult to distinguish from liposarcomas [19–21].

In the acute stage, adrenal hemorrhage appears as hyperattenuating on CT, with attenuation usually measuring 50–90 HU [22, 23]. Although this attenuation may be diagnostic on unenhanced CT, it is indistinguishable from tumor on contrast-enhanced CT (CECT) (Fig. 3A) and therefore may require a follow-up CT examination in 1–2 months to confirm decreased hematoma size and attenuation [24]. MRI can also be used to confirm adrenal hemorrhage, although its appearance on MRI depends on the age of the hemorrhage (Fig. 3B).

Adrenal cysts are rare and can be distinguished from cystic malignancy on CT and MRI if they display no enhancement, near-water attenuation or signal, wall thickness of less than 3 mm, and size no greater than 5–6 cm [25].

Incidental adrenal masses that have nonspecific features on CT and MRI, including metastases, pheochromocytomas, and adrenal cortical carcinomas, cannot be reliably characterized with the use of imaging alone. The imaging features of metastases to the adrenal glands are generally nonspecific and include necrosis (Fig. 4), heterogeneity, density of 10 HU or more on unenhanced CT, slow contrast washout on adrenal protocol CT, no...
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signal dropout on chemical selective MRI, and signal hyperintensity on T2-weighted MR images [26]. \(^{18}\)F-FDG PET frequently is performed during the workup of malignancy and is a very accurate method for differentiating benign from malignant adrenal masses that are larger than 1 cm [27]. Pheochromocytomas typically are large vascular tumors that display avid enhancement on CT and MRI [28, 29]. On adrenal protocol CT, pheochromocytomas usually display slow contrast washout, although, on occasion, they may

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**Fig. 2**—76-year-old woman with left adrenal mass (arrow) incidentally discovered on unenhanced CT performed for abdominal pain. Note significant amount of macroscopic fat throughout mass, which is diagnostic of myelolipoma.

**Fig. 3**—59-year-old man who presented with pain after motor vehicle collision. A, Trauma protocol contrast-enhanced CT image acquired in portal venous phase shows indeterminate adrenal mass (arrow) measuring 3.3 × 2.3 cm (attenuation, 52 HU). B, Six-week follow-up T1-weighted in-phase MR image shows that mass (arrow) has decreased in size to 2.2 × 1.2 cm. Hypointense rim surrounding mass indicates chronic blood products (e.g., hemosiderin).

**Fig. 4**—Two patients with metastatic disease in adrenal gland. A, 62-year-old man with widely metastatic melanoma. Image shows left adrenal metastasis with central necrosis (arrow). B and C, 48-year-old woman with recurrent colon cancer metastatic to right adrenal gland. Contrast-enhanced CT image obtained during portal venous phase (B) shows heterogeneously enhancing indeterminate mass (arrow) (attenuation, 55 HU). FDG PET scan (C) shows significant metabolic activity (arrow) (standardized uptake value, 10.8), which is diagnostic of metastatic disease in this patient with known malignancy.
mimic benign lipid-poor adenomas by showing rapid washout [28, 29]. Although they typically are described as having marked signal hyperintensity on T2-weighted MRI, approximately 35% of pheochromocytomas may have signal hypointensity [30]. Metaiodobenzylguanidine scintigraphy is highly specific for pheochromocytomas and paraganglioma and usually is performed either when there is biochemical evidence of pheochromocytoma without imaging evidence or when searching for metastases [31]. Biochemical testing typically is used to confirm the diagnosis of pheochromocytoma, and cross-sectional imaging is sufficient for tumor localization [31] (Fig. 5). Primary ACC is rare and often is large (> 6 cm) at the time of detection [32] (Figs. 6A and 6B). Imaging characteristics are nonspecific, although heterogeneity, necrosis, and vascular invasion are commonly seen, and calcifications are present in 30% of ACCs [32].

**Imaging and Clinical Guidelines**

The accurate characterization of AIs can be a complex process because of the variety of imaging options available, the frequency of adrenal masses with indeterminate imaging features, and the possibility of hormonal dysfunction in both benign and malignant masses. In an effort to simplify the process, several guidelines have been developed, including those put forth by the ACR in 2010 [2] and 2012 [3], those from the American Association of Clinical Endocrinologists and the American Association of Endocrine Surgeons [4], and those developed by the NIH [5]. Although these guidelines are each thorough and well designed, they are different in perspective and, thus, emphasis. These differences in perspective and emphasis have led to variations in the guidelines, particularly in areas that are subject to expert or consensus opinion because of the lack of large long-term studies.

**Imaging Guidelines**

The major radiologic guidelines include the 2010 white paper of the ACR Incidental Findings Committee [2] and the ACR appropriateness criteria for the imaging evaluation of incidentally discovered adrenal masses, which were published in 2012 [3]. The ACR white paper includes a sample flowchart for the imaging evaluation of AIs (Fig. 7), with the goal of offering the most efficient and effective diagnostic approach to distinguishing benign from malignant masses.

**Clinical Guidelines**

The major clinical guidelines include the 2009 practice guidelines of the American Association of Clinical Endocrinologists and the American Association of Endocrine Surgeons [4], the 2002 NIH Consensus Statement [5], and the expert opinion of Young [33] published in the *New England Journal of Medicine* in 2007. Although mindful of the important role of imaging in lesion characterization, these clinical guidelines place a greater focus on biochemical analysis as a means of follow-up of AIs (Table 1).
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Fig. 7—Flowchart for evaluation of adrenal incidentaloma detected by CT or MRI, as developed by American College of Radiology Incidental Findings Committee. Reprinted from Journal of the American College of Radiology, 7, Berland LL, Silverman SG, Gore RM, et al. Managing incidental findings on abdominal CT: white paper of the ACR Incidental Findings Committee, 754–773, 2010, with permission from Elsevier [2].

Incidental adrenal mass ≥ 1 cm

Diagnostic imaging features

- Myelolipoma, cyst
- No hormonal or imaging follow-up

Adenoma

Prior imaging

- Stable > 1 year

Consider further imaging or resection after hormonal evaluation for pheochromocytoma

Hormonal evaluation

- Functional
  - Consider resection
- Nonfunctional
  - Follow-up hormonal evaluation for excess of cortisol yearly for 4 years if mass is > 2.4 cm

Nondiagnostic imaging features

1–4 cm

- Benign imaging features
  - Presume mass is benign and consider 12-month follow-up CT or MRI

4 cm

- Suspicious or indeterminate imaging
  - Unenhanced CT or chemical selective MRI; perform adrenal washout CT if results still indeterminate

> 4 cm

- Benign imaging features
  - Presume mass is benign and consider 12-month follow-up CT or MRI

- Suspicious imaging features
  - Consider PET or resection

- No history of cancer

Cancer history

No cancer history

Consider biopsy (if history of cancer) or resection (if no history of cancer)

1Benign imaging features = homogeneous, low density, and smooth margins.

2Suspicious imaging features = heterogeneous, necrosis, and irregular margins.

3Noncontrast CT or MRI may alternatively be used to characterize 1- to 4-cm masses in patients with a history of cancer and no prior imaging.

4A 1-mg dexamethasone suppression test (or assessment of 24-hour urinary cortisol level), assessment of plasma (or urine) level of metanephrines, and aldosterone-to-renin activity ratio (if patient has hypertension or a low potassium level).

5Some experts recommend that masses ≥ 4 cm be resected even if nonfunctional, because of increased risk of adrenal cancer, although these guidelines do not distinguish masses with features diagnostic of adenoma [4, 33]. It may be more appropriate for nonfunctional masses ≥ 4 cm with features diagnostic of adenoma to be followed with imaging and with hormonal evaluation [5] or with hormonal evaluation only.

Fig. 8—Modified (from Fig. 7) algorithm for evaluation of incidental adrenal mass detected by CT or MRI, with permission from Elsevier [2].
TABLE 1: Summary of Recommendations From Biochemical Analysis and Follow-Up Imaging Studies of Incidentally Discovered Adrenal Masses

<table>
<thead>
<tr>
<th>Author or Title of Study [Reference]</th>
<th>Publication Year</th>
<th>Hormonal Testing</th>
<th>Frequency</th>
<th>Imaging Follow-Upa</th>
<th>Frequency</th>
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</thead>
<tbody>
<tr>
<td>NIH Consensus Statement [5]</td>
<td>2002</td>
<td>DXT (1 mg) suppression test, assessment of plasma-free level of metanephrines, and evaluation of potassium level and aldosterone-to-renin activity (if HTN)</td>
<td>Yearly for 4 years</td>
<td>Monitor masses &lt; 4 cm</td>
<td>Two CT studies performed &gt; 6 months apart; further follow-up may not be warranted if mass size is stable</td>
</tr>
<tr>
<td>Young [33]</td>
<td>2007</td>
<td>DXT (1 mg) suppression test; assessment of plasma levels of metanephrines and catecholamines, evaluation of plasma aldosterone-to-renin activity (if HTN)</td>
<td>Yearly for 4 years</td>
<td>Monitor masses &lt; 4 cm</td>
<td>CT performed at 6, 12, and 24 months after diagnosis</td>
</tr>
<tr>
<td>AACE and AAES [4]</td>
<td>2009</td>
<td>DXT (1 mg) suppression test, assessment of plasma levels of fractionated metanephrines and normetanephrines or urine levels of metanephrines and catecholamines, and evaluation of plasma aldosterone-to-renin activity ratio</td>
<td>Yearly for 5 years</td>
<td>Monitor masses &lt; 4 cm</td>
<td>Once at 3–6 months after diagnosis and then annually for 1–2 years</td>
</tr>
<tr>
<td>ACR Incidental Findings Committee [2]</td>
<td>2010</td>
<td>May be considered if there are clinical signs or symptoms of adrenal hyperfunction</td>
<td>Once (at time of diagnosis)</td>
<td>Consider follow-up CT or MRI studies if masses are 1–4 cm, if there are benign features, and if prior imaging has been performed, and if there is no history of cancer</td>
<td>Once (at 12 months after diagnosis)</td>
</tr>
</tbody>
</table>

Note—NIH = National Institutes of Health, DXT = dexamethasone, HTN = hypertension, AACE = American Association of Clinical Endocrinologists, AAES = American Association of Endocrine Surgeons, ACR = American College of Radiology. Adapted with permission from [38].

aFor morphologically benign lesions with no hormonal activity.

es that measure 1–4 cm and that have either grown or have retained their indeterminate status after all imaging options are exhausted, in addition to masses larger than 4 cm that occur in patients with a history of malignancy [2, 3]. Conversely, there is general agreement in the endocrinology literature that biopsy should be performed only if knowledge of metastatic disease from a known primary malignancy will affect further therapy. Biopsy cannot reliably distinguish adrenal adenoma from ACC and may be harmful because of the risk of tumor seeding [4, 5, 33, 39].

The second objective of these diagnostic algorithms is to determine the functional status of AIs. Although most patients with AIs have nonfunctioning adenomas (80%), 5–10% have subclinical or early Cushing syndrome, 5% have pheochromocytoma, and 1% have aldosteronoma [33, 36, 37]. The ACR algorithm considers biochemical (hormonal) evaluation, but the document states that routine hormonal evaluation of all incidentalomas “would be costly and is not routinely performed by many physicians” [2]. Furthermore, biochemical evaluation should be considered only “if there are clinical signs or symptoms of adrenal hyperfunction” [2]. This view is contrary to the preponderance of clinical recommendations in the endocrine literature [4, 5, 33, 36, 37, 40].

With the increasing use of imaging, many pheochromocytomas are being detected as AIs rather than as part of a planned evaluation. As many as 12.5% of patients with pheochromocytomas are normotensive, and only 10% present with the clinical triad of sweating, headaches, and palpitations [36]. In one series, adrenal pheochromocytomas were identified as AIs in 19 of 33 patients (58%), and only 10 of these 19 patients had hypertension [41]. However, even clinically silent pheochromocytomas can be lethal [4, 5, 33]. All patients with suspected pheochromocytomas, even those who are normotensive, should be adequately prepared to undergo surgery by receiving α-adrenergic blockade or calcium channel blockers to prevent a hypertensive crisis [4]. Because pheochromocytomas have nonspecific features on imaging, and because clinical expertise in diagnosing pheochromocytomas may vary, it has been suggested that all adrenal masses be screened for catecholamine excess [4, 5, 33]. Plasma metanephrines have similar sensitivity and specificity for pheochromocytoma as urine fractionated metanephrines and may be considered as the first screening test [42].

Subtle, or subclinical, Cushing syndrome refers to the autonomous secretion of cortisol in patients who lack the typical signs and symptoms of hypercortisolism. The prevalence of subclinical Cushing syndrome may range from 5% to 24%, depending on the diagnostic criteria for testing [36, 37], although the true prevalence is likely to be at the lower end of this range [38]. Subclinical cortisol secretion has been associated with hypertension, obesity, diabetes, osteoporosis, and an increased risk of cardiovascular events [33, 43]. There is no general consensus on which diagnostic test is most suitable for the diagnosis of subclinical Cushing syndrome. An overnight 1-mg dexamethasone suppression test for which the posttest serum cortisol level is abnormal (> 5 μg/dL) and the plasma level of adrenocorticotropic hormone suppressed is more sensitive than a 24-hour urinary free cortisol test but is less specific [37, 44].
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Aldosteronomas account for 1% of AIs and have been associated with an increased risk of cardiovascular disease [33]. Hyperaldosteronism, which may occur in as many as 16% of individuals with resistant hypertension, warrants workup to decide whether treatment should involve a mineralocorticoid receptor blockade or resection of a hyperfunctioning adenoma [33, 45]. Hypertension and a low or low-normal serum potassium level may be insufficient screening criteria for hyperaldosteronism [33]. For patients with hypertension and an AI, an appropriate screening test is a random aldosterone-to-renal activity ratio that is greater than 30 [45].

The third objective of these guidelines is appropriate imaging follow-up of AIs with benign characteristics. Consensus guidelines in the endocrinology literature recommend extended imaging follow-up for AIs smaller than 4 cm, even if they are benign and nonfunctioning [4, 5, 33, 40, 43, 46, 47] (Table 1). However, there is a lack of evidence from large long-term studies to support these recommendations [33]. Both benign and malignant incidental adrenal masses may be noted to have enlarged at follow-up. Libé et al. [40] found that 6% of incidental adrenal masses show growth at 1-year follow-up, whereas 14% show growth at 2 years and 29% exhibit growth at 5 years, although that study recorded incidental adrenal mass size without mentioning imaging characteristics. A multicenter study of adrenal adenomas with a follow-up of 5 years or more found that adenoma growth of 1 cm or more occurred in 8.3% of patients and that growth greater than 2.5 cm occurred in 2.4% of patients [43].

The justification for follow-up imaging of AIs with benign characteristics has been patient and physician reassurance through the early detection of growth of malignant masses [5, 33, 37, 38]. Opposing opinions regarding follow-up imaging have been expressed because of the rarity of detection of malignancy on follow-up studies and because of the associated cost and radiation risks [6, 38, 48]. The chance of detecting malignancy during follow-up of benign nonfunctional AIs (0.2% over 2 years) is similar to the predicted risk of the ionizing radiation produced by follow-up CT scans inducing a fatal cancer [38]. Other than the steps required to categorize incidental nodules as benign or malignant, the ACR guidelines do not recommend long-term imaging follow-up. A 1-year follow-up examination could be considered for AIs with benign (but nondiagnostic) imaging features in patients who have no history of malignancy and who have not undergone previous imaging. This guidance is particularly helpful in the common situation of detecting a small (< 4 cm) AI on a CECT examination performed for a patient without known malignancy.

The fourth objective of these guidelines is the biochemical evaluation and follow-up of AIs. AIs may develop cortisol hyperfunction over time, even if they are not hormonally active at the time of the initial evaluation. The risk of a mass larger than 2.4 cm becoming hormonally active is 17% at 1 year, 29% at 2 years, and 47% at 5 years [47]. There is good agreement among the clinical recommendations that individuals with benign nonfunctioning AIs measuring greater than 2.4 cm should obtain annual hormonal testing for Cushing syndrome for 4 years [4, 5, 33]. Other than consideration of initial biochemical evaluation of patients with signs or symptoms of adrenal hyperfunction, the ACR guidelines do not recommend long-term follow-up of hormonal function.

Revised Recommendations

The immediate imaging workup for AI should follow the guidelines proposed by the ACR [2]. Myelolipomas and simple cysts require no additional workup or follow-up imaging. Benign adenomas are characterized by unenhanced CT attenuation of less than 10 HU, signal loss on opposed-phase chemical selective MRI, stable size for more than 1 year (compared with size noted on previous imaging studies, if available), and size less than 4 cm plus imaging features indicating benign status (e.g., homogeneous, low density, and smooth margins) in a patient without a history of cancer [11–14, 49, 50]. If these criteria are not met, CECT with 15-minute delayed imaging is recommended to calculate contrast washout.

For patients with known malignancy, FDG PET or biopsy (performed after exclusion of pheochromocytoma on the basis of results of biochemical analysis) may be helpful in discriminating metastatic disease from benign masses. There is general agreement that surgery should be considered for lesions larger than 4 cm (rather than the previously reported size of 6 cm [5]), which lack the characteristics of benign tumors [33, 36, 37]. Conservative management may be appropriate for patients with limited life expectancy [33]. Rather than supplant the recommendations of the ACR Incidental Findings Committee

<table>
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<th>TABLE 2: Sample Radiology Report Dictation Templates for Common Scenarios Encountered With Incidental Adrenal Masses</th>
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<tr>
<td>Imaging Morphologic and Clinical Findings</td>
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<tr>
<td>Nondiagnostic but benign imaging features* noted on CECT (under the assumption that no prior imaging was performed and there was no known malignancy)</td>
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<tr>
<td>Nondiagnostic but benign imaging features noted on CECT (under the assumption that no prior imaging was performed and there was no known malignancy)</td>
</tr>
<tr>
<td>Features diagnostic for adenoma noted on imaging with unenhanced CT, chemical selective MRI, or adrenal protocol CT</td>
</tr>
<tr>
<td>Features diagnostic for adenoma noted on imaging with unenhanced CT, chemical selective MRI, or adrenal protocol CT</td>
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</table>

Note—CECT = contrast-enhanced CT.

*Benign imaging features of incidentally discovered adrenal masses include homogeneous attenuation, low attenuation, and smooth margins.
[2, 3], we propose a modification of the existing guidelines with respect to biochemical evaluation and percutaneous biopsy (Fig. 5). Most AIs are not hormonally active. However, subclinical hyperfunction has been associated with an increased risk of cardiovascular events, obesity, hypertension, osteoporosis, and diabetes. Performing biopsy or surgery for patients with pheochromocytoma, including subclinical pheochromocytoma, without adequate evaluation and patient preparation may result in a hypertensive crisis. Therefore, all incidentally detected adrenal masses 1 cm or larger should undergo biochemical evaluation, unless the imaging features are diagnostic of a nonfunctional process (e.g., myelolipoma or cyst). In addition to the initial biochemical evaluation, an additional yearly follow-up examination to evaluate cortisol secretion should be performed for masses larger than 2.4 cm or if such an examination is clinically indicated on the basis of new signs or symptoms.

Despite clinical recommendations for prolonged imaging follow-up of adrenal nodules, few data support this practice for a benign nodule without hormonal activity. Biopsy should be limited to patients with a known malignancy for whom AI status remains indeterminate after the imaging options are exhausted, and the knowledge of adrenal metastasis will influence clinical management.

Sample Dictations
Many referring physicians may be unaware of the appropriate imaging and biochemical workup for patients presenting with an AI [10]. The recommendations of the reporting radiologist influence the subsequent adrenal imaging and hormonal workup coordinated by the referring physician [51]. Therefore, we think that the burden is on the radiologist to inform referring physicians of the appropriate recommendations. It would be prudent for diagnostic radiologists to discuss the various recommendations with their endocrinology colleagues to develop a local consensus. Four standard dictations have been developed at our institution to address clinical consensus. Four standard dictations have been developed at our institution to address

Conclusion
The incidental adrenal mass remains a common challenge for radiologists and referring physicians. A complex array of imaging techniques is available to characterize adrenal masses as benign or malignant. Still, even benign adrenal masses may be clinically relevant if they are hormonally active. Significant differences exist among the algorithms developed for radiologic imaging and endocrine evaluation of AIs. This article provides a brief overview of adrenal imaging, emphasizes key differences between the guidelines developed to evaluate AIs, and proposes an algorithm that attempts to bridge these guidelines. Radiologists play a key role in characterizing adrenal masses as benign or malignant and in recommending further imaging and biochemical evaluation for AIs. Until greater agreement is reached in the medical community, it would be prudent for diagnostic radiologists to discuss these topics with their endocrinology colleagues to develop a local consensus.

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